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DISEASES OF INFANTS AND CHILDREN

JOHN PITCH LANDON, M.D., Editor

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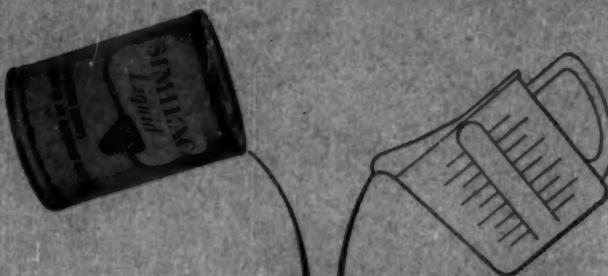
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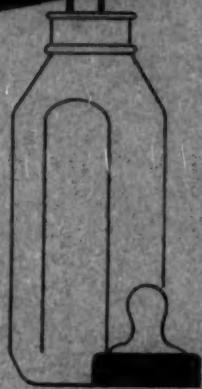
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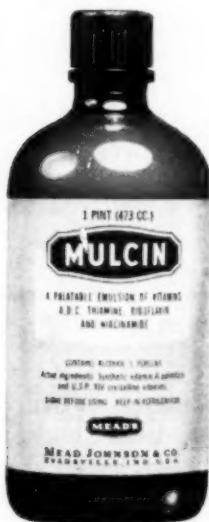
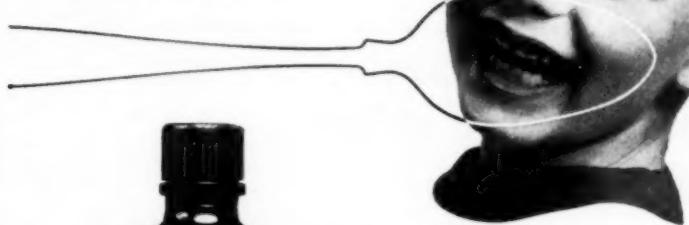


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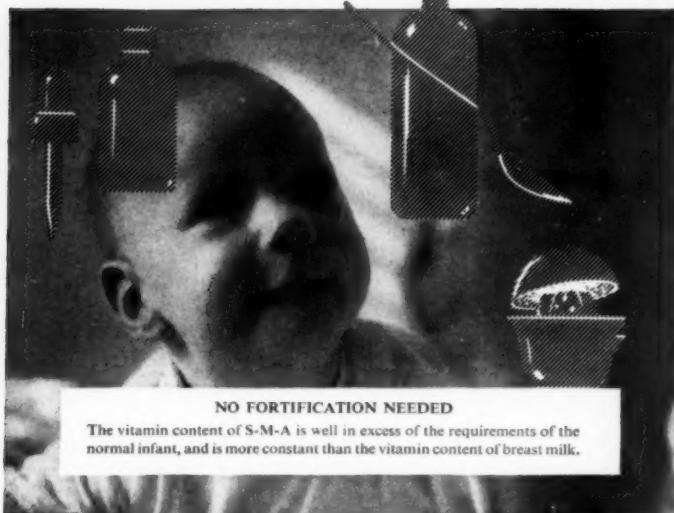
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1. Behrman, H. T., Combes, F. C., Bobroff, A., and Leviticus, R.: Ind. Med. & Surg. 18:512, 1949.





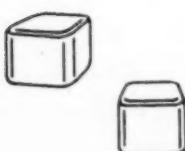
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LÖFFLER'S SYNDROME*

EDWARD H. SCHEER, M.D.

New Britain, Conn.

In 1932 W. Löffler¹ reported a new clinical syndrome of peripheral eosinophilia with associated infiltrations of the lung fields. By 1940 there were approximately 105 similar cases reported in foreign medical literature, 51 of which Löffler² had reported. All of Löffler's cases came from Central Europe.

It apparently was some time later, however, before interest in this syndrome was stimulated in this country. In 1945, when Miller³ reported his case of Löffler's syndrome, he could find only four other case reports in the American medical literature. Since 1945 the amount of material published on Löffler's syndrome and allied conditions has become voluminous.

The standard textbooks of medicine are quite vague in their description of this syndrome. Perhaps one of the most concise descriptions has been given by Ham and Zimdahl.⁴ They listed five diagnostic points which will be given here with additional discussion of each point.

1. Infiltration of the lung fields on roentgenogram: This infiltration may be unilateral or bilateral, spotty or homogeneous, large or small, simple or multiple, and may occur at any site in the lung field.

2. Fleeting and changing character of the infiltration: This is considered one of the most important diagnostic criteria. It was formerly believed that the usual infiltration decreased in size and

*Prepared for Postgraduate Clinical Pediatrics, New York Medical College, Flower and Fifth Avenue Hospitals, New York.

intensity in 3 to 8 days. More recent literature, however, leads one to believe that the infiltrations may persist for days, weeks and sometimes months.

3. Blood eosinophilia: The blood eosinophilia may be only slightly elevated (10-15 per cent) or may be as high as 60 per cent with an associated leukocytosis. The peak of the eosinophilia occurs after the infiltration of the lung fields appears. There is no relation, however, between the degree of eosinophilia and the intensity or size of the infiltration.

Weingarten⁵ states that the eosinophilia in Löffler's is below 60 per cent and uses this as a differential point between Löffler's and tropical asthma, which is supposed to have a much greater eosinophilia (80-85 per cent). Both Miller and Cartwright⁶ have reported cases of Löffler's with as high as 80 per cent eosinophiles.

4. Mild degree of illness: There may be no symptoms of the syndrome—many cases have been discovered on routine chest plate and/or blood count. If symptoms are present they may consist of slight temperature elevation, mild cough (sputum usually absent) and general malaise. On physical examination occasional moist râles may be heard over the lung fields.

5. Short duration of signs and symptoms: The first cases reported proved to be of short duration; however, more recent reports lead one to feel that the duration of the illness may be variable depending upon the severity of symptoms at onset.

The incidence in males has been greater than that in females. In addition to this sex preference there seems to be a definite seasonal incidence for most cases have been reported in July and August.

The etiology of Löffler's still is not definite. Löffler felt that the condition might be an expression of an anaphylactic process or the result of a parasitic infestation. Wild and Loertscher⁷ reported two cases due to ascariasis. Other cases, due to hookworm, trichinosis,⁸ trichuris trichiura, strongyloides stercoralis, microfilariae, trichomonas fecalis, clonorchiasis, amebiasis⁹ and creeping eruption¹⁰ can be found in the literature.

In making the diagnosis of Löffler's one of the most important conditions to be ruled out is pulmonary tuberculosis. Löffler did tuberculin tests on his cases and found that 35 per cent had negative tests. One case later developed tuberculosis.

Other conditions to be ruled out in making the diagnosis are Hodgkin's disease, periarteritis nodosa and eosinophilia leukemia.

In an attempt to determine the incidence of Löffler's syndrome with parasitic infestation, all cases of parasitic infestation admitted to the Pediatric Ward of the Metropolitan Hospital, New York City, for a two-year-period from May 1949 to May 1951, were reviewed. The findings will be found in Chart 1.

CHART 1.

Pt.	Age	Sex	C.C.	Parasite	Eosin.	Chest	Tuberculin
W.P.	4	M	URI	Ascaris Trichinura	none	not done	Vollmer neg.
R.F.	11	M	Wt. loss, cough	Trichinura Hookworm	not done	normal	Mantoux 1:100 neg.
O.M.	3	M	URI	Trichuris Ascaris	not done	normal	Vollmer neg.
W.G.	4	M	Fracture	Ascaris	not done	clouding at 1st rt. ant. intercostal space	Mantoux 1:1000 neg.
A.P.	3	M	Diarrhea	Ascaris Hookworm Trichuris	2%	not done	Vollmer neg.
R.G.	2½	M	Passage of Ascaris	Ascaris Trichuris	not done	normal	Vollmer neg.
D.P.	7	M	int. parasites	Ascaris Hookworm Trichuris	9%	normal	Vollmer neg.
G.P.	3	F	URI	Trichuris Hookworm	5%	density rt. base	Mantoux 1:1000 neg.
S.C.	11	M	Anemia ? dwarfism	Hookworm Schisto- soma Trichuris	1%	normal	Vollmer neg.
V.R.	9	M	URI	Trichuris	not done	normal	Vollmer neg.
R.G.	11	M	Anemia	Hookworm Schisto- soma Trichuris	10%	normal	Vollmer neg.
R.F.	6	M	Diarrhea	Trichuris	not done	not done	Vollmer neg.
A.C.	8	M	Wt. loss, Diarrhea	Trichuris	none	normal	Mantoux 1:1000 neg.
C.B.	8	F	Abd. pain	Trichuris	4%	normal	Mantoux 1:1000 neg.

R.G.	8	F	Cough & fever	Hookworm Schistosoma Trichuris	3-12%	density rt. base	Vollmer neg.
E.G.	9	F	Anemia	Hookworm	2%	cloudy patch 2nd left interspace	not done
R.R.	5½	M	Fever, abd. pain, passage of worms	Ascaris Trichuris	4%	patchy clouding lower pole rt. hilus	Mantoux 1:1000 pos. (primary Tbc)
D.A.	10	M	Fever, nausea, cough	Ascaris Trichuris	55%	increased lung markings radiating to base, bilat.	Mantoux 1:100 pos.
R.M.	2	M	Retarded develop.	Ascaris	14%	not done	Vollmer neg.
G.N.	1½	M	URI-pneu.	Ascaris	11%	RUL pneu.	Mantoux 1:100 neg.
J.A.	8	M	Diarrhea	Trichuris	not done	normal	Mantoux 1:100 neg.
G.P.	7	M	? Anemia	Hookworm Trichuris	2-16%	atelect. RUL	Mantoux 1:1000 pos.
L.L.	6½	M	Cough	Hookworm Trichuris	not done	normal	Vollmer neg.
R.V.	11	M	Abd. pain	Trichuris	none	normal	Vollmer neg.
J.Z.	2½	M	Tbc. workup	Trichuris	not done	blunting left costophrenic sinus ? effusion	Mantoux 1:10,000 pos. (pul. tbc.)
A.R.	11	M	Acute nephritis	Trichuris	6-9%	normal	Mantoux 1:10,000 pos.
I.V.	5	F	Cough, fever	Ascaris Trichuris	3%	hilar densities	Mantoux 1:1000 pos. (pul. tbc.)
L.C.	10	M	Cough, night sweats	Ascaris Hookworm Trichuris Schistosoma	11%	increased density rt. infra-clavicular area	Mantoux 1:100 neg.
A.N.	4	F	URI	Ascaris Trichuris	not done	not done	not done
V.D.	3	M	URI	Ascaris	not done	not done	Vollmer neg.

A.A.	10	M	URI	Hookworm	7%	normal	Vollmer neg.
R.G.	8	M	Anemia	Trichuris	none	not done	Vollmer neg.
O.R.	2	F	? celiac	Ascaris	2%	normal	Mantoux 1:10,000 neg.
				Trichuris			
M.M.	13	F	Boarder	Trichuris	none	normal	not done
I.T.	6m	M	Abd. pain	Strongyloides	none	normal	Vollmer neg.

DISCUSSION

In the 35 cases there were 11, of 28 who had chest plates, who showed pulmonary infiltrations. Twenty-four of the 35 had differential counts and of these 12 showed greater than 4 per cent eosinophiles. Seven of those with chest infiltrations had over 4 per cent eosinophiles; 2 had no differential done, and 2 had 2 per cent and 3 per cent eosinophiles. Two of the cases proved to be bronchopneumonia; 3 pulmonary tuberculosis, and 6 were asymptomatic and undiagnosed. Of the 6 undiagnosed, 2 had positive Vollmer patches, 3 negative Vollmer's or Mantoux and 1 had no tuberculin test done. The lung infiltrations in all 6 patients cleared without specific therapy. Thus of the 35 cases reviewed, at least 3 can be considered Löffler's and an additional 3 cases are questionable Löffler's syndrome.

It would seem that the appearance of lung infiltrations depends on whether these patients with parasitic infestations develop an allergic response to the protein of the parasite.

COMMENT

In addition to Löffler's, two other syndromes of eosinophilia and lung infiltrations have been reported by other authors. One of these is tropical asthma¹¹, described by Weingarten, and the other, visceral lesions associated with extreme eosinophilia reported by Zeulzer and Apt.¹² It would seem that all three syndromes might be considered varying degrees of the same condition. Löffler's is the least severe; tropical asthma has greater respiratory symptoms; and the syndrome described by Zuelzer and Apt is the most severe for here, in addition to the allergic response in blood and lungs, we have the same response in spleen and liver (most pro-

noticed in the liver). Further experience and study will no doubt prove these are all stages of one disease.

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99 West Main Street.

RELATION OF BIRTH WEIGHT AND CONTROL. (Archives of Disease in Childhood, London, 25: 380, Dec. 1950). Illingworth and associates had demonstrated earlier that the birth weight of a child bears an important relation to his subsequent weight and height. In the studies reported here, they tried to determine whether children with different birth weights differ in all the standard body dimensions. They measured the weight, standing and sitting height, pelvic girth, chest and calf circumference in 238 children, aged 5 to 8 years, of three birth weight groups: 5 lb. 8 oz. (2,494.76 Gm.) or less, 7 lb. 2 oz. (3,231.84 Gm.) to 7 lb. 6 oz. (3,345.24 Gm.), and 8 lb. 8 oz. (3,855.53 Gm.) or more, and analyzed them by statistical methods. It was found that in all measurements the children of the lowest birth weight groups were smaller than those of the largest birth weight group, the measurements of the children of average birth weight falling in all cases (except in sitting height) between the two.—*Journal A.M.A.*

THE EFFECT OF AN ANTIHISTAMINIC SUBSTANCE (PYRIBENZAMINE) ON ERYTHEMA NEONATORUM*

HAROLD LEVY, M.D., F.A.C.P.

AND

ALAN B. BAGNER, M.D.

Brooklyn.

Erythema neonatorum has received relatively little attention in the pediatric literature because of its benign course. However, the controversial nature of its etiology has provided some interesting treatises, notably those by Mayerhofer¹ and Lehndorff.² The varying theories are indicated by the names that have been bestowed upon the condition. The older authors used erythema papulatum, Leiner used toxic erythema of the newborn and subsequently Mayerhofer¹ named it erythema neonatorum toxicum and propounded the theory of allergy which caused Urbach³ and Von Reuss⁴ to suggest the name "erythema neonatorum allergicum." Lehndorff² gave an excellent review with further evidence of the allergic theory in a general consideration of allergy in the newborn. He uses the term erythema neonatorum and it seems the most convenient and descriptive.

The condition is seen in otherwise healthy newborn infants and is characterized by edema of the eyelids, erythema of the cheeks, patchy erythematous macules of the thorax, abdomen and extremities, varying in size from 2 mm. to 3 cm.; other children show a morbilliform eruption of the thorax, abdomen and extremities. Clinically, the eruption appears to be otherwise asymptomatic—there is no fever, no itching or other obvious discomfort and no loss of appetite or disturbance of sleep⁵. It is interesting to note that the incidence of the condition in Mayerhofer's group of 1,500 newborns was 46 per cent, while our own figures (in 1,750 newborn infants) show less than 5 per cent. We are not able to explain the reason for this difference of 41 per cent. It may be that he included cases with milder eruptions in his statistics.

Mayerhofer's theory of allergy for the pathogenesis of the condition seems sound. It states that toward the end of pregnancy, various proteins formed in the maternal organism (pregnancy

*From the Nursery Service, Menorah Maternity, Beth-El Hospital, Brooklyn, N. Y.
Material used in this study was supplied through the courtesy of Ciba Pharmaceutical Co.

toxins, hormones and others) may go through the placenta and into the fetal organism; the latter would eliminate them with the help of the placenta, but while in the fetus an allergy against the before mentioned maternal protein substances would be initiated. However, allergens created during pregnancy which have been transmitted to the body in the last hours before its birth can no longer be taken care of by the placenta and are not excreted. These remain in the organism of the already allergic newborn and will produce immediate reactions, consisting of the eruption of the erythema neonatorum.

It was further pointed out by Meyerhofer that this theory could not be proven fully by clinical observation despite the fact that it explained all the known peculiarities of erythema neonatorum. Only one observation could be taken to be in favor of the theory of allergy and that was the fact that two-thirds of the newborn infants examined during the eruption of the disease showed eosinophilia. Schick* found eosinophile cells in purulent vesicles of the eruption.

Before attempting to test this theory it was felt that one further factor had to be considered because the eyelids were swollen and the rash usually appeared first on the cheeks and seemed to spread down the body. This was the possibility that the erythema might be due to the application of silver nitrate used for ophthalmic prophylaxis. To determine this as the cause, the left cheek of each of 104 infants, born in a two week period, was anointed immediately after delivery with sterile petrolatum jelly from the nose to the ear, and from the eye down to the mandible. The silver nitrate solution was then instilled into the eyes. Five cases with erythema neonatorum were observed, in each of which both cheeks were equally involved indicating that the silver nitrate was not the cause of the dermatitis.

In order to prove the allergic nature of the eruption, an anti-histamine substance, elixir Pyribenzamine⁸⁻⁹ was tried as treatment. For the purpose of this investigation, the first case was treated with a 5 mg. dose four times daily, and the next case with a 10 mg. dose four times daily, and the third case was not treated and used as a control. This was continued in the same order without selection until there were 25 cases in each group.

During the period of this study, there were 1,649 live births.

*Dr. Bela Schick, personal communication.

Seventy-five cases of this type of dermatitis were observed, an incidence of 4.5 per cent.

In this study of 75 cases, results were not affected by birth weight, which ranged from 5 pounds 6 ounces to 9 pounds 15 ounces. The severity, distribution and comparative occurrence of the condition is outlined in Table 1. The various grades were spread throughout the three groups of cases, and it was interesting to note that the clinical response in the treated cases was not affected by the severity of the eruption.

TABLE 1

Grade I	Distribution		No. of Cases
	Eyelid edema alone.....	
Grade II	Eyelid edema with facial involvement.....	30
Grade III	The above plus eruption on the thorax and frequently the abdomen.....	18
Grade IV	The above plus involvement of the extremities.....	17

The results of treatment are summarized in Table 2. The first group of 25 cases are those treated with 5 mg. four times daily. The duration of eruption ranged from 1 to 4½ days with an average of 2.3 days until the skin was clear and the average total dose of medication was 44 mg. with range of 20-90 mg.

TABLE 2

	No. of Cases M F	Range of Birth Wt.	Range		Average Duration to Clearing	Range of Duration
			Average Dose mg.	Dose mg		
5 mg. dose	15 10	5 lbs. 8 oz. 9 lbs. 3 oz.	44	20-90	2.3 days	1-4½ days
10 mg. dose	12 13	5 lbs. 6 oz. 8 lbs. 12 oz.	77.6	40-120	2.1 days	1-3 days
Control	11 14	6 lbs. 9 lbs. 15 oz.			4.5 days plus	2½-5 days plus

The second group of 25 cases are those treated with 10 mg. four times daily. It took an average of 2.1 days until the eruption

cleared with a range of 1-3 days, and the average total dose of medication was 77.6 mg. with a range of 40-120 mg.

The third group of 25 cases were untreated and served as controls. The average duration of the eruption until clearing was in excess of 4½ days. The exact duration could not be calculated because 3 babies went home in 5, 5 and 4 days, respectively, with the eruption still present.

No evidence of toxicity was noted due to the medication. The infants continued to take their feedings regularly. Gastro-intestinal disturbance appeared in three cases on the 10 mg. dose who regurgitated or spit out the medication immediately. It was found that when the dose was diluted with water it was well tolerated.

SUMMARY AND CONCLUSION

1. A skin eruption in newborn infants called erythema neonatorum has been considered an allergic condition.
2. It was demonstrated that prophylactically instilled ophthalmic silver nitrate does not produce the eruption.
3. Assuming the allergic nature of the eruption, an antihistaminic (elixir Pyribenzamine) was used for treatment.
4. A controlled series of 75 cases occurring in a series of 1,649 live births (an incidence of 4.5 per cent) was studied. In those treated with Pyribenzamine 10 mg. four times daily the condition cleared up in 2.1 days, whereas the control cases cleared up after more than 4½ days. The quicker disappearance of the rash indicates that our assumption of the allergic nature of erythema neonatorum seems to be correct.

The authors wish to express their gratitude to Dr. Bela Schick, Acting Consultant in Pediatrics, for many suggestions in this study.

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750 St. Marks Avenue.

CLINICAL OBSERVATIONS ON EARLY ADMINISTRATION OF POLYVITAMIN SOLUTIONS TO NEWBORN INFANTS*

JOSEPH SCHWARTZMAN, M.D.

MADELEINE E. MORCY, M.D.

DAVID BRAND, M.D.

AND

CORNELIUS H. NAU, M.D.

Brooklyn.

Although studies have been published¹⁻³ on the use of vitamins for full term and premature infants, and although recommendations have been made favoring water soluble vitamins⁴⁻⁶, the questions of tolerance and indications during the first few days of life are still unsettled.

To determine these factors, two water soluble multivitamin preparations^{x, y} were selected. Amounts varying from 0.2 cc. to 0.9 cc. were given to 809 full term white and colored newborn infants on the day of birth. The dosages were measured by a graduated dropper and administered by the nurse directly into the infant's mouth. The same dosage was continued daily until the babies were discharged from the hospital. Their weights at birth and on discharge were compared to determine the amounts gained or lost. In addition, notations were made on the occurrence of any skin eruptions. A control group of 415 white and colored newborn infants was similarly observed. In all other respects, the

x. Supplied under the trade name of ViSyneral through the courtesy of the U.S. Vitamin Corporation, New York, N. Y.

This product had the following composition. Each 0.6 cc. provides:

Vitamin A (natural).....	5000 U.S.P. Units
Vitamin D (natural).....	1000 U.S.P. Units
Ascorbic acid (C).....	50 mg.
Thiamin (B-1).....	1 mg.
Riboflavin (B-2).....	0.4 mg.
Niacinamide	5 mg.
Pyridoxine (B-6).....	0.1 mg.
Pantothenic acid.....	2.0 mg.

y. Supplied under the trade name of ViPenta through the courtesy of Hoffman-LaRoche, Inc., Nutley, N. J.

This product had the following composition. Each 0.6 cc. provides:

Vitamin A (synthetic).....	5000 U.S.P. Units
Vitamin D (activated ergosterol).....	1000 U.S.P. Units
Ascorbic acid (C).....	50 mg.
Thiamin (B-1).....	1 mg.
Riboflavin (B-2).....	0.5 mg.
Niacinamide	10 mg.

*From the Department of Pediatrics of New York Medical College, Flower and Fifth Avenue Hospitals and Metropolitan Hospital, New York.

infants received identical care and feeding. The results are summarized in Table 1.

TABLE 1. Results of the Administration of Multivitamin Preparations to Newborn Infants.

	x Product	y Product	of x & y Totals	Controls
Average stay in hospital (days).....	5.45	5.55	5.50	5.55
Number of patients.....	487	322	809	415
Number losing weight.....	346	200	546	321
Percentage losing weight.....	71.05	62.11	66.58	77.35
Average loss (ounces).....	4.99	3.75	4.37	5.15
Number gaining weight.....	121	105	226	78
Percentage gaining weight.....	24.85	32.6	28.73	18.8
Average gain (ounces).....	3.04	3.01	3.03	3.39
Number of stationary weights.....	20	17	37	16
Number with skin eruptions.....	57	32	89	31
Percentage with skin eruptions.....	11.7	9.9	10.8	7.47

DISCUSSION

Most types of milk, including human and cow's milk, are deficient in the components of vitamin B complex^{1,7,8} and in ascorbic acid⁹. Since infants require not only vitamins A and D, but also C and B complex factors for optimum growth and development, it would seem that the addition of multivitamin preparations to the feedings would most easily supply the deficits. In using these products, the question arises whether they should be begun on the day of birth of the infants. If so, what would be the advantages or disadvantages.

In reviewing the tabulated data, it can be seen that both multivitamin preparations reduced the average initial weight loss of the babies. Both solutions also increased the percentage of infants that showed gain in weight by the fifth day. Although the average weight gained was about the same for all the infants, a larger number showed this gain when the multivitamins were administered. The number of generalized skin reactions and eruptions about the buttocks were more frequent with both preparations as compared to the controls.

It would seem that the use of multivitamins for newborn babies from the first day of birth increased the percentage of infants who did not show an initial loss of weight as compared to the control group. The only deterrent to the use of the aqueous

polyvitamin solutions was the frequent appearance of skin eruptions. In the latter cases, it might be advisable to discontinue the preparations concerned or else substitute similar combinations of vitamins made by other procedures. However, in the main, it would appear as though the majority of the babies benefitted to some degree from the early administration of multivitamins.

SUMMARY

1. Newborn infants were given aqueous solutions of multivitamins from the day of birth until the day of discharge from the hospital.
2. Two preparations were selected at random.
3. Although all the infants that gained weight showed approximately the same weight gain, however, the administration of the polyvitamins reduced the percentage of newborn infants that showed an initial weight loss.
4. The occurrence of skin eruptions was increased.

CONCLUSION

Although aqueous multivitamin preparations were not tolerated as well during the first week of life as contrasted to their later use, their administration however increased the number of newborn full term infants that did not show an initial weight loss. Therefore, in those babies who tolerate these preparations and do not develop any skin reactions, polyvitamin preparations can be utilized as an additional aid in diminishing the amount of initial weight loss and reducing the number of losers.

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1747 West 2nd Street.

BANTHINE IN PEDIATRICS*

A PRELIMINARY REPORT ON SENSITIVITY, TOXICITY AND DOSAGE

REUEL A. BENSON, M.D.

JOSEPH SCHWARTZMAN, M.D.

MARVIN GREEN, M.D.

AND

HOLLEY W. REED, M.D.

New York

Among the newer treatments for peptic ulcer is the anticholinergic drug, Banthine^{1,2} (B-diethylaminoethyl xanthine 9 carboxylate methobromide). Up to the present time, it has been used primarily in adults. However, since it is becoming generally known that peptic ulcers also occur in infants and children³⁻⁸, this drug should be useful in their treatment. Moreover, since the drug has been effective in the control of vagotonia and parasympathotonia, it should be of value in other conditions that are precipitated or aggravated by the increased flow of stimuli through these segments of the autonomic nervous system.

However, since Banthine has not been used to any extent in pediatrics, it was felt that the drug should first be studied for sensitivity, toxicity and tolerated dosage.

Intradermal tests were performed on 367 children using 0.5 mg. per dose (0.1 cc. of 5 mg. of Banthine per cc.) and of these, 3 gave a positive skin reaction. This consisted of at least 1 cm. of induration with or without surrounding erythema. Two children manifested systemic reactions and one developed both local and general signs. Of this group, 48 negative cases were retested one month later and one of these now gave a positive test lasting two hours. Thus, of a total of 415 children tested, 5 (1.2 per cent) developed positive skin tests indicating a local sensitivity and 2 (0.5 per cent) exhibited systemic manifestations suggesting a general sensitivity or a total of 7 reactions (1.7 per cent) for this group. Seven of the children tested were diagnosed as atopic dermatitis but no local or general reactions occurred in any of these.

Among the positive reactors, two had areas of induration with

*From the Department of Pediatrics of New York Medical College, Flower and Fifth Avenue Hospitals and Metropolitan Hospital, New York.
Banthine was furnished through the courtesy of Dr. Irwin C. Winter, Clinical Director of G. D. Searle and Co., Chicago, Ill.

erythema that measured more than 1 cm. in diameter and lasted about 2 hours. Of these patients, one had been negative when first tested but became positive when retested. No systemic toxic signs were noted. Two others had similar local reactions which lasted more than 12 hours but without any systemic manifestations. The other three had systemic manifestations resembling atropine-like effects with an erythematous flush, tachycardia, irritability, dryness of membranes and pupillary dilatation with sluggish reaction to light. In only one of these was this reaction pronounced but it disappeared within 12 hours. In only one was a positive skin test noted while the other two presented systemic signs only. One of the latter two patients was retested and no reaction at all was noted. However, upon retesting the first one, a positive skin test was still obtained but without any general toxic manifestations.

These results indicated that skin testing for sensitivity was not a consistent indicator as to the expectancy of systemic reactions.

Eighty-five conjunctival tests were done using one per cent Banthine solution (50 mg. in 5 cc. of distilled water) and mydriasis occurred in 63 within an hour and rarely lasted longer than 48 hours. No inflammatory reactions were noted.

Its effect was then compared to that of one per cent homatropine, the Banthine being instilled into the right eye and a similar amount of homatropine into the left eye. It was noted that the homatropine was more effective with respect to rapidity and duration of dilatation. In addition, 5 patients had Banthine solution instilled into both eyes and these were contrasted to 5 similar aged patients who had instillations of the homatropine solution. The results still favored the homatropine. Since several of the patients used in this study were those who were local or general reactors, it was felt that the conjunctival test was no criterion as to this drug's sensitivity.

Following this, it was decided to determine the dosage that could safely be used for infants and children.

Seven newborn infants, whose intradermal skin tests were negative, were given Banthine orally. The medication was started on the second neonatal day with a dosage of 12.5 mg. This was increased to 12.5 mg. twice a day in 7 cases and then further increased to three times a day in 3 cases. In one female infant the drug was discontinued because of three vomiting episodes but it could not be

determined whether it was due to the Banthine or persisted despite its use. Another male infant on the three times a day schedule had a typical atropine-like reaction with a temperature of 102° F., flushing of the skin, mydriasis and a cardiac rate of 180 per minute. Within 3 hours the reaction had subsided. Another 2-week-old female infant, who also had a negative skin test, was given 12.5 mg. three times a day for 4 days. During that period, she vomited frequently, had a temperature of 99° to 100.5° F. (rectally) and widely dilated pupils. On the fourth day, the pulse became rapid and feeble and the medication was discontinued. Eleven days later she was given 6 mg. three times a day for several days with no untoward reaction.

Three other infants under one year of age were started with 12.5 mg. of Banthine twice a day and gradually increased to 25 mg. four times a day with no evidence of sensitivity.

Four children, ranging from 1-3 years, were similarly treated with the dosage being increased to 50 mg. four times a day with an occasional facial flush as the only unusual finding. Two other children, over 1 year of age, were started with 50 mg. three times a day and one child 3 years old was given 50 mg. four times a day for about 6 weeks with no evidence of toxicity.

Five patients were also given parenteral Banthine. Three infants, 4, 6 and 8 weeks of age, respectively, were given the medication subcutaneously. The 8-week-old infant received 6 mg. to 12.5 mg. every 6 hours without any reaction and the 4-week-old infant was given 12.5 mg. to 25 mg. every 6 hours with no evidence of local or general reaction. However, the 6-week-old infant, who had a slight rhinitis, received 12.5 mg. every 6 hours and following the second dose developed an erythematous flush. Medication was skipped for one day and then restarted. After the fourth dose, a temperature of 102°F. with evidence of a wheezing chest and an erythematous flush appeared and therefore medication was terminated. Several days later, this infant was given oral Banthine 12.5 mg. four times a day for 2 days, 25 mg. four times a day for 2 days and then 50 mg. four times a day for 24 hours. Flushing of the skin and dilatation of the pupils were noted with the latter dosage and medication was again discontinued.

A 16-month-old child, with a negative skin test, was placed on 25 mg. of Banthine every 4 hours subcutaneously, and after the

second dose a marked flush appeared. Medication was discontinued for one day and then resumed with no ill effects after 4 consecutive doses. This infant was then given an oral dosage of 25 mg. four times a day for 2 days, 50 mg. four times a day for 2 days, and then 75 mg. four times a day for 1 day. With the latter dosage dermal flushing was again noted and no further medication was attempted.

One of the skin-negative children in the 1 to 3 year group, who had flushing with the 50 mg. oral dose, was placed on 25 mg. every 6 hours parenterally. However, systemic manifestations developed and this necessitated discontinuing the drugs.

A number of the infants and children were kept on the Banthine for from one to twelve months depending upon their stay in the hospital. Monthly or every other month, a study of blood sodium, potassium, chloride, sugar, urea, icteric index, Van den Berg, cephalin flocculation, cholesterol and protein were done but there was no evidence of any physiologic disturbance. In addition, no urinary or blood count changes were detected, but in most instances the pupils were dilated. In three of the cases, dermal flushes were noted at one time or another. Parenteral medication was associated with a much higher reaction rate than with the oral route.

Since the dosage was approximately determined and the toxicity was negligible, it was decided to apply the medication clinically. Three cases of pyloric stenosis were treated with no noted improvement in two, but the third seemed to benefit somewhat from the therapy.

Case 1. B. V., a one-month-old male with a typical history and symptomatology of pyloric stenosis, was placed on parenteral Banthine. Every 6 hours 12.5 mg. were given for 6 doses and then increased to 25 mg. for another 12 doses. The patient continued to vomit and since an x-ray revealed a characteristic picture, surgery was resorted to and the stenosis was corrected.

Case 2. L. V., a 6-week-old male with a typical course of pyloric stenosis, was placed on 12.5 mg. four times a day orally for 2 days. Vomiting decreased in frequency, but the amount of each vomitus increased. This retention vomiting was probably due to the fact that there was little or no effect on the hypertrophied pylorus but there was relaxation of the walls of the stomach. In

view of the lack of improvement, surgery was decided upon and a typical pyloric stenosis was found and corrected.

Case 3. O. R., a 2-month-old female infant with a history of failure to gain weight since birth with vomiting after most feedings, was x-rayed and prolonged gastric retention observed. Thick frequent feedings and sedation did not achieve much improvement. The patient was placed on parenteral Banthine and was given 12.5 mg. every 6 hours for 10 doses. Vomiting ceased on the same day that the drug had been started. The medication was stopped and vomiting recommenced and continued for 2 days. The drug was given again and 6 mg. was administered subcutaneously every 6 hours for 4 days with cessation of vomiting. As soon as the Banthine was stopped, the vomiting started again. Surgery was deemed advisable at this point, and a definite pyloric stenosis was discovered and corrected.

One case of diarrhea was given Banthine as a supplementary medication. C. F., a 4-month-old female infant, was admitted with a history of 7 watery stools during the two days prior to admission. In addition, an acute tonsillitis was present. Besides the routine diarrhea therapy, 12.5 mg. of Banthine was given orally four times a day for 3 days. During this period only one loose stool was noted.

Banthine was also utilized in one case of vomiting. G. M., a 10-month-old infant, was admitted with a history of vomiting of everything ingested for the previous 24 hours. She was given 12.5 mg. of Banthine orally four times a day for 3 days. During her hospital stay, there was no vomiting at any time.

DISCUSSION

Banthine, a drug, which gives great promise in the treatment of peptic ulcer of adults, may also be applied to similar conditions in children.

The question of dosage arises and, from the work done thus far, it can be stated that children tolerate the drug relatively better than adults. Moreover, the dosage cannot be calculated according to any rigid rules but must be individualized for each patient. Approximate dosage ranges, however, can be recommended.

1. In newborn infants, it would appear desirable to start with not more than 12.5 mg. every 12 hours and then increase the frequency to every 8 hours.

2. In those infants from 1 to 12 months of age, Banthine should be started with a dosage of 12.5 mg. four times a day and increased gradually to 25 mg. four times a day.

3. In children over one year of age, the dosage should vary from 12.5 mg. to 50 mg. four times a day.

4. In parenteral dosage, it is advisable that one-half the recommended oral dose be used. In our experience, Banthine, given parenterally, produces more frequent and more severe reactions, although in no instances were the toxic manifestations observed considered to be of serious nature.

Skin and conjunctival tests were done but in reviewing the histories of those who had positive skin tests, only one had a systemic reaction. Of the systemic reactors, only one had a positive skin test. This would tend to indicate that both of these tests are of negligible value in determining generalized sensitivity to this drug.

Up to the present, clinical experience with the drug has been limited to three pyloric stenosis cases of which one showed some doubtful response to Banthine, with no beneficial results in the other two at all; in one case of diarrhea and another of vomiting, the drug may have been helpful to a certain degree. However, it could not be clearly evaluated because it was used as an auxiliary measure and because of the inadequate number of cases.

Further studies are being carried out in the treatment of enuresis, adiposity and functional vomiting in hypertonic infants.

SUMMARY AND CONCLUSIONS

1. Banthine was skin tested on 415 cases and 5 had local and 2 had general reactions.

2. Eighty-five conjunctival tests were done.

3. Both of the above tests were of no value in detecting untoward reactors to Banthine.

4. Dosages for the different ages were approximated and general recommendations are made.

5. It was noted that children tolerate the drug well and no blood, renal or liver disturbances were observed.

6. Parenteral medication should not exceed half the recommended oral dose since it resulted in more severe reactions.

7. Banthine did not show much promise in pyloric stenosis but it may prove to be of value as a supplementary measure in vomiting and diarrhea.

8. Banthine has wide potentialities but must be tried clinically in a larger series before any conclusions can be drawn.

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RAPID EFFECT OF PENICILLIN ON *TREPONEMA PALLIDIUM*. (*Münchener medizinische Wochenschrift*, Munich, 92: 1427, Dec. 8, 1950). A male infant, aged 23 days, with congenital syphilis, was treated with penicillin (crystalline procaine penicillin G and buffered crystalline potassium penicillin G) in aqueous solution. The initial dose was 2,500 units twice daily, which was increased to 10,000 and 20,000 units. The total dose administered was 95,000 units. A pronounced Jarisch-Herxheimer reaction, with icterus, general deterioration and rise of temperature, required discontinuation of the antibiotic when the cutaneous manifestations were about to subside and permanent improvement was to be expected. Circulatory collapse and death occurred on the thirteenth day of treatment. Necropsy was performed, including microscopic examination of the heart, lung, liver, kidneys, thymus, pancreas, spleen and head of the left humerus, which had been tender and could be moved only with difficulty during life. Levaditi's silver nitrate staining method was used for *Treponema pallidum*, which could not be demonstrated in any of the organs examined. Syphilitic osteochondritis was observed in the left humerus, but the transition of granulation tissue into cicatricial tissue in the calcification zone at the epiphyseal line suggested that healing of the bone lesion had started. Results showed that the numerous spirochetes present in congenital syphilis disappear rapidly after the administration of even relatively small doses of penicillin. Prevention of congenital syphilis in infants by prophylactic treatment of mothers is stressed.
—*Journal A.M.A.*

RITUAL CIRCUMCISION

HARRY APFEL, M.D.*

Brooklyn, N. Y.

Ritual circumcision has been the subject of controversy for many years. According to Genesis it had its beginning when Father Abraham received the mandate from God: ". . . Every man child among you shall be circumcised" (Genesis 17, 10). The children of Israel have been steadfast in the observance of this mandate all through the ages. Throughout the years of their exile the Jews endured untold oppression under many inhuman rulers who outlawed ritual circumcision. Many of the Roman emperors, notably Aelius Adrian, exacted severe penalties for the infraction of the decree forbidding its performance (History of the Jews-Graetz). In modern times and under liberal governments, we frequently read the appellation, the "circumcised," a term applied with intent to degrade the particular individual.

While in the beginning the practice of circumcision was based on a religious creed and was being observed largely by the children of Abraham, today the Christian world has come to appreciate its hygienic and prophylactic benefits. What was once regarded as a stigma of a minority group and as an act of mutilation has since come to be accepted as an important rung in the ladder of preventive medicine. Science and rational thinking has triumphed over intolerance and bigotry. Some translate this to read "democracy in action."

Thus far I have stated general and accepted facts to which no contradictions need be anticipated. One does not expect the same easy sailing from the paragraphs to follow. There is always the possibility of being misunderstood. This is not unusual whenever a radical change in any phase of life is suggested. This is especially true where the subject matter is so closely tied up with old-established customs and deeply rooted traditions. The reader of this article is asked, most humbly, that he keep an open mind and without bias reflect upon the idea involved and reserve judgment upon the facts to be presented.

As a basis for our discussion I will advance two questions, namely, Is ritual circumcision satisfactory? Can ritual circumcision be performed while at the same time observing modern sur-

*Chief of Pediatrics, Unity Hospital, Brooklyn, N. Y.

gical principles and without in the least violating the covenant between God and Abraham (Genesis 17, 9)?

The answer to the first question needs no equivocation. Anyone engaged in the practice of medicine is bound to meet with the untoward consequences following ritual circumcision. While these mishaps are not fatal, they, nevertheless, bring about untold suffering to the newborn infant and mental anguish to the parents of the little patient.

To treat the second question properly some qualification is necessary. The Bible tells us the first circumcisions were performed by the patriarch Abraham upon the male folk of his household in accordance with the mandate from God. The Jewish laws, formulated and handed down from generation to generation, made it mandatory upon every Jewish father, that he himself, circumcise his newborn son when he reaches the eighth day of life. As the scholars entrusted with the interpretation of that law realized that not every father will have the courage or the dexterity to carry out this precept, they inserted a clause that permits the father to designate someone else to perform the operation. As time went on, the circumcision technique was handed down from one to another by an apprenticeship. At the present time the person who is engaged in this calling is named a "mohel" (literally, a cutter). These men are recognized as "professionals" and licensed by the constituted religious leaders in Judaism. The technique employed by these professional "cutters" is a modification of the technique that was in vogue 50 years ago. It would serve no purpose to describe in detail the crude technique employed by our forebears. Their results were productive of local and systemic infections quite frequently. Recently, an article was published which I have read with great interest, which states in part as follows: "any danger in connection with ritual circumcision which may have existed in the past has been entirely eliminated." I wish this statement were true. Unfortunately, the author's opinion is not based on existing hospital case records. In my daily hospital rounds, I frequently find babies which have sustained ugly granulating wounds and others that require surgical treatment in order that the bleeding may be controlled, following ritual circumcision. Many of these results are remedied by members of the hospital staff without ever bringing them to the attention of the babies'

parents. Open criticism from members of the medical staff is apt to bring about uncomplimentary reaction from certain religious groups. The parents of the little patients invariably throw their sympathy in favor of the religious side. The hospital executives are helpless in this matter for experience has shown that no good would be obtained by replacing one mohel with another, since these "professionals" have all had the same training. Our State University and Board of Regents do not make it obligatory that these "cutters" obtain the accepted courses in medical sciences and hospital internships compulsory for anyone who wishes to practice surgery. A mohel does not have to pass examination in any of the basic medical sciences, e.g., anatomy, pathology, etc. It is superfluous to remind the lay reader that circumcision is surgery. It may also be underscored that modern surgery makes no distinction between one form of surgery and another. Every surgical case is to be regarded with the same importance and must be treated with the same surgical principles. The safety and security of human life makes these rules inflexible.

A Plea to Remedy This Existing Problem. It is obvious that neither organized medicine nor the State can bring about the necessary change in this undesirable problem by a stroke of the pen as it were. The necessary reform can only be brought about by the constituted religious leaders of our community. As previously stated, the rabbis have already sanctioned some modification from the old and crude technique. If, in the judgment of the rabbis, they found it permissible to modify the original technique, why not carry the thought a step farther and permit an all-surgical technique? A surgical technique need not encroach upon the religious services which form part of the ritual circumcision. The patient's family may engage a rabbi of their choice in order that he may officiate in accordance with custom and tradition at the same time that the doctor is performing the surgery.

For the benefit of some readers, it may be underscored that in Judaism many of the traditions and sacred mandates, while they are being strictly observed by some, have recently come to be greatly "streamlined." To illustrate this point, one or two examples may be cited. The Bible makes the observance of the Sabbath rest one of the strictest Hebrew laws. It is, as all know, the fourth commandment of the Decalogue. There are entire Jewish

communities in our own country who observe this law to a letter, while at the same time we find some men and women, members of highly respectable Jewish congregations, who at the same time carry on their routine activities on the Sabbath day. The Mosaic Dietary Law is another very important law to be observed in Judaism, and as everyone knows, many of our best Jewish families enjoy pork chops and Virginia ham in their menus. Our religious leaders apparently do not disapprove of the infraction of the above laws. It is also a known truth that the Jewish law is very liberal to permit modification of any tradition where the health of the individual is concerned. The progress made in modern medical and surgical science should be sufficient to convince our leaders in Judaism that ritual circumcision deserves that it be given the desired change to conform with the principles of modern thought.

CONCLUSION

Abraham and his followers, for many years, performed circumcision the way they understood in their time. In the course of these many thousands of years medical research with the help of Almighty God, opened man's eyes and enabled him to appreciate the knowledge obtained from the study of the sciences. Should we deny the benefits of that knowledge to our newborn babies, that God created "in His own image"?

I would ask the persons who have honored me by reading the above lines to believe in my utter honesty and sincerity of purpose. Should this article fail to bring about the results desired, I will accept it as the best judgment of the day. I will continue to hope, nevertheless, that some time in the near future some one wiser and more capable will again take up this work in order to bring about this highly important and worthwhile change.

884 Park Place.

CLINICAL REVIEW

In order to encourage the writing of clinical articles by recent graduates or senior medical students, the ARCHIVES will publish monthly at least one such paper from the classes of Doctor Reuel A. Benson, New York Medical College, New York, and Doctor Philip Moen Stimson, Cornell Medical School, New York. Other interested medical schools are cordially invited to submit student papers for consideration.

TREATMENT OF THE NEPHROTIC PHASE OF CHRONIC GLOMERULONEPHRITIS WITH ACTH*

REPORT OF TWO CASES

ALLAN B. AINLEY, JR., M.D.
Valhalla, N. Y.

Much has been reported on the use of ACTH in many and varied conditions, but relatively little has appeared evaluating the use of this drug in the nephrotic syndrome.

The purpose of this report is to present the results in two cases of the nephrotic syndrome in children treated with ACTH on the Pediatric Service at Morrisania Hospital, New York.

CASE REPORTS

Case 1. This 18-month-old negro male was admitted with a two-weeks history of generalized swelling of the face and a three-day history of generalized swelling of the body and legs. The mother stated on admission that prior to the day of onset of symptoms the child did not void during the entire night. One week prior to onset the patient suffered a mild afebrile upper respiratory infection. A history of frequent head colds with fever was obtained. A history of an acute episode of nephritis or of a previous similar attack could not be elicited. The review of the birth and development of the child revealed no abnormalities. The family history and resumé of systems were non-contributory.

Physical examination revealed an 18-month-old infant in no acute distress, exhibiting lethargy, anasarca and abdominal distention. Positive physical findings were injection of the nasopharynx with mucopurulent discharge, small shotty anterior cervical lymphadenopathy, slight injection of the ear drums and shift-

*Submitted as partial fulfillment of the requirements of the course in Senior Pediatrics at the New York Medical College, Flower and Fifth Avenue Hospitals, New York.

ing dullness in abdomen. Temperature 99.4° F., pulse 100, blood pressure 90/66 weight, 29 pounds.

The laboratory on admission showed:

Hb. 11 gms	Urine: s.g. 1.040
R.B.C. 4.1 M	albumin 4 plus
W.B.C. 6,400	sugar negative
Diff.—polys 26%	casts—rare hyaline and gran-
lymphs 64%	ular casts
E.S.R. (Cutler) 12/60	Occas. R.B.C. and W.B.C.

See Table 1 for blood chemistries.

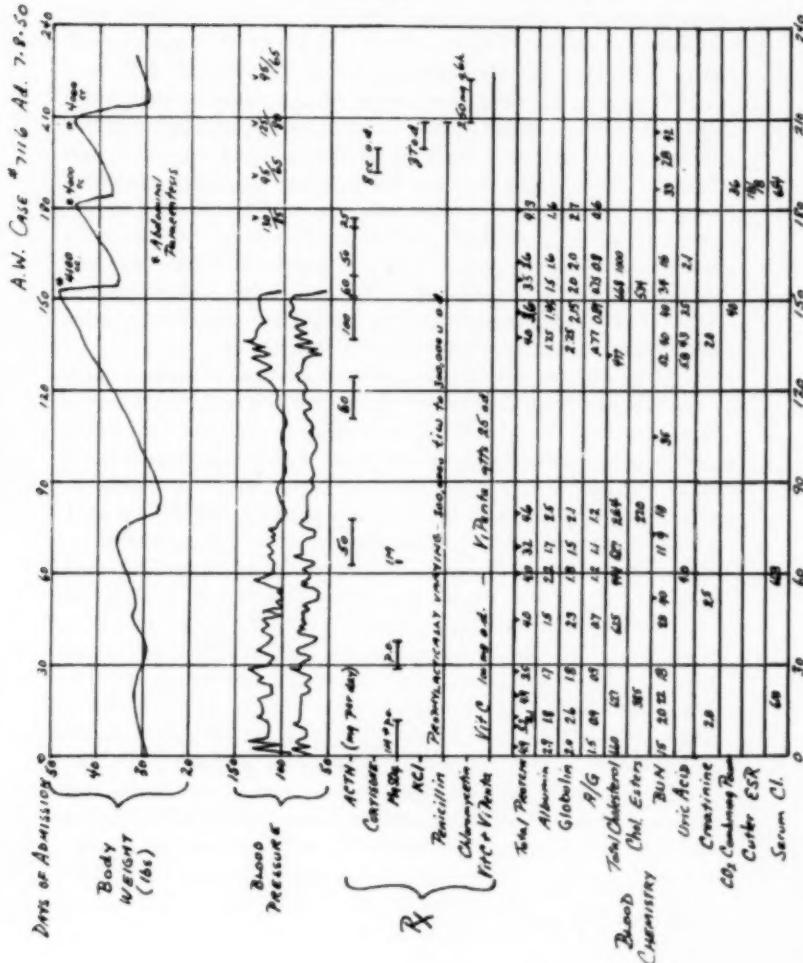
Admission diagnosis was nephrotic stage of chronic glomerulonephritis.

Therapy ordered on admission consisted of Lanolac, salt free diet, multivitamin drops, vitamin C, penicillin prophylactically.

Subsequent to admission the patient's systolic blood pressure ranged between 115 and 130; magnesium sulfate therapy was instituted per os and intramuscularly for 11 days without marked effect on the child's fluctuating blood pressure. (Table 1). On the 17th day of admission patient was placed on a Kempner diet (salt-free, rice, fruit juices) in addition to Lanolac. Systolic blood pressure readings exceeding 130 were noted on the 27th day of admission and prompted another trial of magnesium sulfate per os for 8 days. On the 29th day following admission a modified Schiff diet was started. For the first forty days of hospital confinement body weight remained static and the clinical condition unchanged, but this was followed by a steady accumulation of fluid and increase in weight (Table 1).

On the 63rd day, with a body weight of 35 pounds (6 pounds above admission weight), child was placed on a 15-day course of ACTH (50 mg. daily in two divided doses intramuscularly). On the 10th day of this régime diuresis ensued and patient lost 8 pounds over a period of one week. This was reflected clinically by the disappearance of periorbital edema, a decrease in abdominal distention and a general increase in alertness. The loss of fluid also resulted in a lowering of blood pressure. This remission was shortlived and was followed closely by a steady reaccumulation of fluid (Table 1) and the return of periorbital edema and marked ascites. On the 110th day of admission the child weighed 35½

TABLE # 1



pounds and another course of ACTH (60 mg.o.d.) was instituted lasting 14 days; this had no effect whatever on the progressive gain in weight. On the 136th day, body weight reached 40½ pounds and another 14-day trial of ACTH (100 mg.o.d.) was given; this was likewise without benefit. Following this third ACTH course, the drug was continued at reduced dosages until the 177th day (see Table 1). On the 152nd day child weighed 47½ pounds and was markedly edematous and distended and showed signs of respiratory distress due to the pronounced ascites. An abdominal paracentesis was performed with the removal of 4,100 cc. of fluid. Following this procedure body fluid rapidly recollected in spite of the continued ACTH therapy and necessitated another paracentesis on the 182nd day with removal of 4,000 cc. of fluid. Once more fluid quickly reaccumulated and on the 191st day an eight-day trial of Cortisone (8 cc. o.d., I.M.) was given without clinical effect on the course of the disease. Signs of respiratory distress occurred again requiring a third abdominal paracentesis on the 208th day of admission with the removal of 4,000 cc. of ascitic fluid. At the time of this last procedure the child weighed 45½ pounds and then 37½ pounds following the withdrawal of fluid. On the 215th day the body weight was 29½ pounds suggesting that a spontaneous remission occurred following the paracentesis. On the 230th day, the last day of observation covered by this report, the patient weighed 32 pounds and the clinical status was approximately the same as on admission.

On the 216th day of observation the patient spiked a temperature of 103° F. and it was noted on physical examination that the left ankle and leg were swollen, hot and tender. A diagnosis of deep cellulitis was made. The prophylactic penicillin therapy was stopped and the child placed on chloromycetin 250 mg. q. 6 h. Response was rapid and the leg appeared normal and temperature was normal in 48 hours. Laboratory work: During hospitalization daily urinanalyses were done with the following average results:

s.g. 1.020-1.040

albumin 3-4 plus

sugar negative

W.B.C. rare to a few per hpf.

R.B.C. rare to a few per hpf.

casts none to a few hyaline, fatty and granular casts

On the 148th and 149th days following admission, macroscopic hematuria was noted which subsided spontaneously.

Blood chemistries performed during observation are recorded on Table 1.

Case 2. This two-year-old white male was admitted with a three-day history of upper respiratory infection and puffy eyelids. Child apparently was in good health until three days prior to admission when he developed a rhinitis; at this time mother noticed a puffiness of the upper and lower eyelids which progressively increased until the time of admission. The past history revealed that the child suffered frequent head colds and had bronchitis one month prior to admission for which he had received penicillin and sulfa therapy. Birth and development were normal. Family history and review of systems were non-contributory.

Physical examination showed a well-developed, well-nourished alert white male in no acute distress, temperature 99.8° F., pulse 116, blood pressure 120/60, respirations 26, exhibiting puffiness of face and generalized swelling of body. The following positive physical findings were observed: bilaterally injected ear drums, diffusely inflamed pharynx, tonsils moderately enlarged and injected, shifting dullness percussed in abdomen, 1 plus pretibial edema.

Laboratory work on admission showed the following:

W.B.C. 11,800	Urine: s.g. 1.041
Diff.—polys 32%	albumin 4 plus
lymphs 65%	sugar negative
monos 3%	occas. R.B.C.
B.U.N. 27 mg.%	occas. W.B.C.
	rare hyaline cast

Admission diagnosis was nasopharyngitis, bilateral acute catarrhal otitis media and nephrotic phase of chronic glomerulonephritis.

Therapy ordered on admission consisted of salt-free diet, multi-vitamins, vitamin C, penicillin prophylactically.

Following admission patient was active and the course generally not remarkable except for a gradual increase in body weight from 30 pounds on admission to 38 pounds on the 24th day following admission; this was reflected clinically by increasing abdominal

distention and periorbital edema. Systolic blood pressures were generally higher as fluid accumulated, reaching 125 at times. (see Table 2.)

On the 17th day post-admission, a course of ACTH (15 mg. q.i.d., I.M.) was instituted lasting fourteen days. After seven days of this ACTH therapy diuresis ensued and child's body weight began to fall rapidly until on the thirteenth day of therapy a weight of 26 pounds was reached—a loss of 12 pounds of fluid in six days. This remission was only temporary, however, and a gradual increase in body weight followed. During the remission, periorbital edema disappeared and abdominal distention was decreased. Systolic blood pressures were generally lower, ranging about 95.

On the 24th day of admission patient spiked a temperature of 102° F., and physical examination revealed an inflamed pharynx and coarse rhonchi throughout both lung fields; penicillin was increased to 100,000 units q. 6 h. and the upper respiratory infection responded within 48 hours.

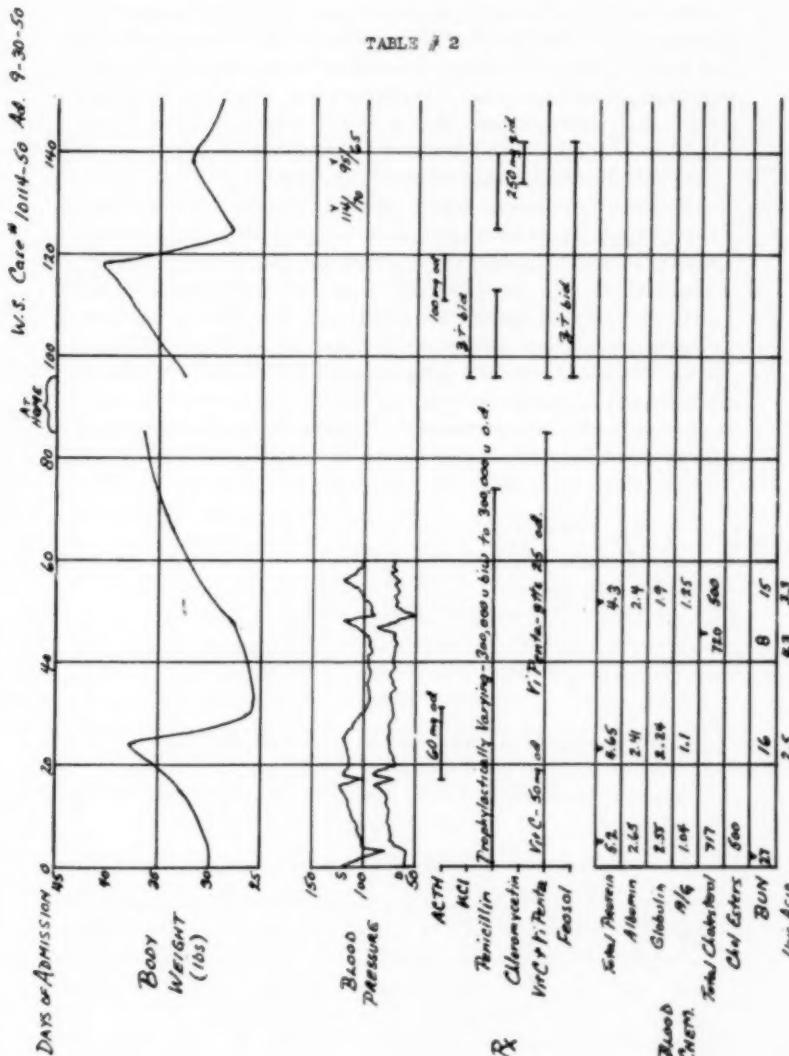
In spite of continued prophylactic dosages of penicillin child spiked a temperature of 104° F., on the 69th day post-admission due to an acute upper respiratory infection; this episode likewise responded to an increase of penicillin dosage to 100,000 units q.i.d.

On the 84th day of hospital observation patient weighed 36½ pounds; moderate periorbital edema, abdominal distention and pretibial edema were present, and child was afebrile. At this time patient was released for a ten-day visit home.

Upon readmission ten days later child exhibited congested nose and mild pharyngeal injection and a temperature of 101° F. Body weight 32½ pounds. Penicillin was administered 100,000 units q. 6 h. and a rapid response resulted; penicillin was then continued at prophylactic levels.

On the 111th day following original admission, child weighed 37¾ pounds, and a second course of ACTH (100 mg. o. d., I.M.) was started lasting nine days. On the seventh day of therapy with a body weight of 40½ pounds, diuresis began, and a loss of 12 pounds in fluid occurred over a period of six days.

On the 130th day of observation child began spiking a temperature which reached 103° F. on the 133rd day. Physical examination revealed pharyngitis and an acutely diffusely tender abdomen



with marked voluntary spasm; an area of angry periumbilical erythema was noted, and a diagnosis of peritonitis was presumed. A leukocytosis of 15,600 was present with an absolute increase in polymorphonuclear cells. Penicillin was given 100,000 units q.2 h. and chloromycetin 250 mg. q.4 h. On the 139th day temperature was normal and abdominal findings had disappeared. The antibiotics were discontinued two days later.

Following the second course of ACTH (nine days) ending on the 120th day post-admission, child weighed 28 pounds and periorbital edema disappeared and a decrease in abdominal distention was evident. On the 138th day a gradual accumulation brought patient's body weight to 32 pounds and this was followed by a spontaneous loss of weight so that on the 150th, or last day of reported observation, the child weighed 29 pounds. At this time child's clinical appearance was essentially the same as on original admission 150 days previously. Laboratory work: During hospitalization daily urinanalyses were done with the following average results:

s.g. 1.024—1.041
albumin 3-4 plus
sugar negative
micro.—few to occas. R.B.C. per hpf.
occas. to many W.B.C. per hpf.
casts—none to occas. hyaline, granular
and pus casts.

The appearance of casts was sporadic and suggested no trend toward progression or remission of the disease.

Blood chemistries performed during hospitalization are recorded on Table 2.

RESUMÉ OF CASES

In Case 1 it is seen that the patient apparently responded with diuresis on the first ACTH course (50 mg. o.d.), the response occurring on the 10th day of the 15 day regimen. This remission was temporary and reaccumulation of fluid prompted another course of ACTH followed by a course of Cortisone, both of which produced no response whatever. Following the first course it is seen that blood pressures and blood chemistries (Table 1) also

tended to approach more normal values: Total protein 4.6 gms.% ; albumin 2.5 gms.% ; globulin 2.1 gms.% ; A/G 1.2; total cholesterol 264 mg.% ; cholesterol esters 220 mg.% ; blood urea nitrogen 10 mg.% . However, this favorable change was also shortlived as indicated by tests performed at later dates. The clinical picture of the child at the time of last observation was essentially no different than that observed upon admission.

In Case 2 it is seen that the child responded with loss of fluid on two consecutive trials with ACTH, the first 60 mg.o.d. for 14 days and the second 100 mg.o.d. for 9 days. The remissions so induced both occurred on the seventh days of their respective courses. Blood pressures and chemistries were done only during the first trial, but it is seen that there was no appreciable change in chemistries following that course. Blood pressures, however, did respond favorably to the loss of fluid. Neither remission was permanent; however, a slight exacerbation following the second remission was succeeded by a spontaneous remission. At the time of last observation the clinical picture of the patient was approximately the same as upon admission.

CONCLUSIONS

The data presented suggests that ACTH is capable of inducing in this disease a temporary diuresis and loss of accumulated fluid with an accompanying drop in blood pressure but that this response is not invariable. The remissions occurring in the reported cases occurred *during* the course of therapy. Furthermore, in these two cases ACTH apparently had no marked effect on the correcting of blood chemistries and probably had no effect on the chronic nature of the disease or on the ultimate outcome.

DISCUSSION

The mechanism of the action of ACTH in inducing a remission in the nephrotic syndrome is quite unknown. From what is known concerning the action of the adrenal cortex the use of this substance would appear to be theoretically contraindicated. Deming and Luetscher suggest that adrenal cortical overactivity plays some part in the etiology of the syndrome and that through the administration of Cortisone an aggravation of clinical findings occurs which is followed by a secondary depression of the adrenal cortex and diuresis *after* the drug is discontinued. These investi-

gators employed Cortisone on 11 nephrotics of varying ages. In five cases there was no effect; in the other six temporary remissions were induced lasting variably from days to months. They stress, however, that the remissions occurred only after the course of the drug was finished. This was not the situation in the herein reported cases; remissions occurred here during therapy. Although ACTH was employed rather than Cortisone, it would seem logical to expect similar results from both.

The Pharmacy and Therapeutics Committee of the University of Michigan Medical Bulletin states that the nephrotic syndrome responds to ACTH by the retention of water and electrolytes followed by a diuresis *after* discontinuance of therapy. It is seen that our observations are again at variance with the latter report.

SUMMARY

Two cases of the nephrotic syndrome in children were treated with ACTH. Temporary remissions were induced but there is no evidence that such therapy in any way altered the underlying unknown etiology or the pathology, course or outcome of the disease.

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Grasslands Hospital.

ACUTE TOXIC GASTROENTERITIS TREATED WITH CONSTANT INTRAVENOUS DRIP INFUSION. (Ugeskrift for Laeger, Copenhagen, 112: 1607, Nov. 16, 1950). Constant intravenous drip infusion given to 47 infants with acute toxic gastroenteritis resulted in rehydration in two to 11 days in 44 cases; three patients died. The average period of hospitalization was 38 days. Infections elsewhere in the body were demonstrated in 15 cases. In 37 cases, including the three fatal cases, penicillin was given alone; in five cases it was combined with sulfonamide preparations and in four with aureomycin. The temperature became normal on the sixth day on the average and gain in weight began on the tenth day on the average. The clinical picture in one of the fatal cases was similar to that seen in crush syndrome.—*Journal A.M.A.*

PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

OCCURRENCE AND MORTALITY OF TYPHOID FEVER IN INFANTS AND CHILDREN*

HENRY KOPLIK, M.D.
New York.

It is interesting to note the erroneous ideas prevalent as to the occurrence, frequency and severity of course of so common a disease as typhoid fever in the infant and child. The physician who has passed through several epidemics of typhoid fever cannot reconcile his own observations with those usually accepted on this subject.

It is now generally acknowledged that typhoid fever can be conveyed from the mother to the fetus. The infection in a majority of cases occurs by way of the placenta and in a large percentage of cases causes the death and premature expulsion of the fetus. If, however, the fetus is carried to term it is born infected with the disease and dies soon after birth with symptoms closely resembling a sepsis of the newly born. Gerhardt, Jacobi, and Blumer have published such cases and the literature on this subject has since been enriched by the observations of Morse, Blackader, and Crozer Griffith.

The disease in the newly born runs an atypical course, the infection partaking of the nature of a hematogenous one. The classical symptoms of typhoid fever are absent in these very young patients. The mortality is very high.

Typhoid fever occurs later in early infancy, that is, up to the age of two years, beyond the question of a doubt. Here also we must separate the cases of infantile typhoid before the age of twelve months from those occurring up to the age of two years. Cases belonging to both periods are fast accumulating in the literature since attention has been called to this important subject by the writings and discussions of Northrup, Griffith, Wilson and

*Read before the Eastern Medical Society of New York City, March 13, 1903.
Reprinted from ARCHIVES OF PEDIATRICS, 20:335-340, May 1903.

others. If some doubt must be thrown on the older literature of typhoid fever in infants and young children up to the end of the second year of life, we must in all fairness admit that an observer such as Henoch was not far wide of the mark when he published 9 cases of typhoid fever in infants and children below the age of two years in a series of 381 cases. Some of the cases in the older literature cannot be unreservedly accepted as those of typhoid fever, inasmuch as at that time laboratory methods, especially the serum diagnosis and the examination of the feces for typhoid bacilli, were not in vogue. Today with the aid of more exact methods of diagnosis we have been able to establish the truth of the contention of early writers that typhoid fever certainly does occur in children below the age of two years, though not with as great a frequency as at a later period of childhood. The causes of this infrequency can readily be explained on external grounds. During the first year and most of the second year of life the infant and young child is fed with food which has been subjected to heat to a greater or lesser extent. Such children, it must be assumed become infected either through food or by coming in contact in some uncleanly way with the infectious material.

It has been shown by me how in a family of children convalescents from typhoid with ambulatory and apparently mild types of typhoid fever may infect others. Thus there is nothing to prevent the younger children of a family from being infected. I must conclude also from my own observations that these younger children have a marked susceptibility to infection. I have noted elsewhere the infection of a child in my own ward with typhoid fever. This patient had been in my ward under observation suffering from another affection. In this case I am still at a loss to know how, in a hospital with all the precautions exercised in a children's ward against the occurrence of infection, it could have taken place. The infectious material must have been infinitesimal. This only illustrates that infants and children have a great susceptibility to the disease and will contract it if occasion presents. We cannot as yet state in figures the frequency of typhoid fever in infants and children below the age of two years as compared to that of older children and adults, until a sufficient number of cases have been observed and diagnosed with modern methods.

In a very recent publication Koch shows that in a certain locality of Germany the children were the chief sources of infection in the dissemination of typhoid fever and also that the average physician failed to diagnose typhoid fever in the children of the village. Koch asked for the school lists and on investigating the absent children he found 72 cases of typhoid fever among the absentees. Of these 72 cases only 8 had been diagnosed and reported as typhoid fever; whereas, the remaining cases on being examined as to the presence of typhoid bacilli in the feces and by the Widal reaction were found to have typhoid fever though clinically they were treated for other maladies.

The mortality among infants and children below the age of two years cannot as yet be stated with accuracy. It is, however, I think, larger than is generally appreciated, if a series of cases in epidemics of varying severity are taken into consideration. Griffith has collected a number of cases below the age of one year; and though we must look with doubt on many of these cases drawn from the early literature, still he has shown that the mortality is fully 50 per cent.

As we pass the second year of life the mortality will diminish, for, according to statistics of Curschman, for children between the age of two and five years this is only 4 per cent. We will refer to these statistics later. I have reason to believe that this favorable figure can only be true of mild epidemics, for Marfan in the epidemics observed by him in early childhood has encountered a mortality of 50 per cent.

If mortality in adults is studied from the age of adolescence, the fifteenth year to that of forty, we see that, according to Curschman the average mortality varies from 8.7 per cent to 14.9 per cent in epidemics of ordinary severity. In severe epidemics such as those recorded by Liebermeister and others the mortality has, at times, risen as high as 20 to 40 per cent. We cannot speak understandingly of the mortality of typhoid fever in adults without taking into account the periodic appearance of a series of severe cases as well as the general run of a moderately severe type. The age of the patient must also be taken into account, for the older the patient, apparently the greater the mortality in the adult. Olser, in a series of 829 adult cases, gives a mortality of 7.5 per cent without stating the various ages and their

respective mortality. If we consider the mortality in children from the ages of two to ten years, we at once see that various authors differ in their mortality rates according to the method by which these figures were collated. Thus Stowell in a series of 61 cases, 4 of which were under two years of age, did not lose a case. Forchheimer, of Cincinnati, in a series of 80 cases did not lose one. Baginsky in an epidemic of 50 cases did not lose one. Thus here is a series of 190 cases and no mortality. On the other hand Henoch in a series of 381 consecutive cases had a mortality of 13 per cent. This author, however, emphasizes the fact that in some years he did not lose a single case. At other times the severity of the epidemic caused the death of a large number of children. From this standpoint, therefore, Henoch is inclined to look with doubt on the statement of some that typhoid fever in children is always a mild disease. For completeness sake it is well to note that Ashby and Wright in a series of 592 cases had a mortality of 8 per cent and Comby in 250 cases a mortality of 7 per cent. Curschman, giving the statistics of a large number of cases occurring in Hamburg, shows that in the year of 1886 the mortality was 7.3 per cent in the children as compared to 11.5 per cent in the adult. In 1887, 6.8 per cent in children as compared to 8.8 per cent in the adult. Of 152 cases of typhoid fever in the adult treated in the Mount Sinai Hospital in the years 1898-1900 there was a mortality of 9.2 per cent as compared to a mortality during the same years in the children's service of 6.6 per cent. Thus in cases drawn from the same epidemic there was only a difference of 2.2 per cent in the mortality rate. In this same series of cases the mortality in 1898-99, in 29 cases was 10 per cent, and in 1899-1900 in 31 cases it was only 3 per cent with practically the same treatment.

Of the American authors both Holt and Griffith make the mortality low. Holt took 2,603 cases of twelve different observers and found a mortality of 5.4 per cent. This method of collating the cases of various observers necessarily includes cases both mild and severe, and does not give an idea of the varying mortality. My own experience does not support the view that typhoid fever is always a mild disease in children from the age of two to ten years. Of 100 cases I have had series, for example 1900 and 1902, in which I have had a mortality of 3 per cent; whereas, in former

years, the mortality mounted as high as 10 per cent in the same service. This year in a series of apparently mild cases we had the most severe complications, namely, two of perforation. In children there is little reaction due to toxemia and a severe intoxication runs to outward appearances a mild course. The children are, however, severely ill, the emaciation is rapid and sometimes extreme. If we study the cases we will see that in these so-called mild cases the most severe complications may ensue. It is deceptive to say, therefore, that typhoid fever is mild in any particular case because the child does not seem very ill. Certain it is that, if we study the statistics of the general run of cases of Henoch, Baginsky, Curschman and those I have noted from my service, the mortality varies from 6.6 per cent to 13 per cent from the age of two to ten years. Whereas, in the adult as seen in the statistics of Osler and Curschman the mortality is not much higher. Children in severe epidemics are subject to a mortality of 30-40 per cent if the toxemia is great.

The causes of the mortality in children are much the same as in the adult. The greatest number die of toxemia, the next greatest number die of hemorrhages, pneumonia, and perforation. That perforation is not uncommon in children is distinctly shown by Mery who states that in the last six years a dozen cases of perforation have been observed in children in the hospitals of Paris. These perforations occurred for the most part in the beginning of the third week of the disease, and were preceded in most cases by hemorrhage. The mortality in perforation was shown by Mangin to be 67 per cent. Of the series of 829 adult cases of Osler there was perforation in 23 cases, a percentage of 2.7 per cent.

Curschman in a very large series of cases met with perforation in from 1.6 per cent to 2.2 per cent. This writer quotes, however, some very unfavorable statistics, including those of Murchison, giving 21.2 per cent of perforation; of Hesch, who in 1,271 autopsies found 4.06 per cent of perforations, and of Bouardel and Thoriot, who in 1,721 autopsies, found 11.3 per cent of perforations. These large figures are probably only true of certain severe sets of cases.

In my own experience I have met 2 cases of undoubted perforation, one of which was operated upon, in a series of 100 cases.

On the other hand Filatow has never seen a case. Henoch's series of 381 cases includes only one of perforation. The heart, of all the organs, though undoubtedly affected in most cases by the toxemia and fever, does not present the severer forms of myocarditis or endocarditis. I must conclude from my own observations that these complications are rarer than in the adult.

Typhoid fever in the fetus and newly born, as far as the reported cases show, is a very severe, and in most cases, a fatal infection. In infants and children below the age of two years, the real mortality is still a matter of speculation on account of the lack of reliable statistics. From the age of two to ten years the mortality varies according to the severity of the epidemic. In some years the mortality is very low (Stowell, Forchheimer, Baginsky). At other times the mortality will mount as high as 6 to 13 per cent, varying with the age and severity of the infection. In some epidemics of a particularly virulent type, the mortality has risen to 20 to 40 per cent (Marfan, Baginsky). It is thus for practical purposes not well to mass cases, inasmuch as the mortality in a severe epidemic is cut down by the favorable results in a moderately severe type of the disease.

RESPIRATORY OBSTRUCTION DUE TO THYMUS. (*Acta Chirurgica Scandinavica*, Stockholm, 100: 466, Dec. 5, 1950). A case of rapid growth of the thymus in an infant with severe respiratory obstruction is described. Transpleural extirpation gave complete freedom from symptoms. The removed thymus weighed 50 Gm. and showed a histologically normal picture. Probably the enlargement was due to rapidly progressing hyperplasia. No other case of equally rapid growth of the thymus has been found in the literature. It is one of the few cases in which an unquestionable connection has been established between thymus enlargement and respiratory difficulties in an infant. It is suggested that in such cases the symptoms may be due to the rapid growth of the thymus rather than to its actual size.—*Journal A.M.A.*

PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

NERVOUS EXHAUSTION IN INFANTS*

W. P. NORTHRUP, M.D.
New York.

It was said that a baby of four months, living in a neighboring city, was slowly fading away; that if something was not done for it soon, it would be too late. The history as related by the mother was substantially as follows: For the first three months the baby was a good sleeper and ravenous feeder, particularly happy and strong. It was stated that he was a good-natured baby, would wake from sound sleep and smile, at any hour, day or evening, for callers. It was nursed at its mother's breast and she had milk enough.

My presumption was that the young mother's milk was now failing, that judicious feeding would soon put the child into good condition, the mother would go home happy, and with her my reputation brilliantly enhanced. A naturally strong baby, wet-nursed through the fourth month, seemed to present an easy feeding problem.

The first look at the mother showed a naturally strong, but worn-out, thin and pale young woman. She had recently been through a strenuous horse-show week, trying at the same time to entertain a houseful of friends and to nurse her baby; and she looked it. The baby, too, looked thin, white, but very alert. It jumped at any noise, smiled spasmodically, twitched, had dark circles under its eyes. The mother, with most engaging smile, declared he was the brightest, best-natured and strongest baby in her city. She said he slept all night, and nursed every time she offered him the breast.

After its journey it was, of course, tired but still alert. The mother said: "He was very cunning in the train (seven hours); he never closed an eye, looked at everybody and everything, visited

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all about the parlor car, entertained everybody and was pronounced the best-natured baby ever seen."

A sunny south room was provided for baby and nurse, the entire third floor constituting the hospital. A baby carriage and Walker-Gordon modified milk were waiting, and I may say the entire domestic and professional plant of my house was at the service of this bit of humanity. Incidentally, I may add, it strongly resembled in appearance one of the average inmates of the Marasmus Room of the New York Foundling Hospital.

At sight, my courage suffered a severe shock. On this case there hung many hopes and incidentally my reputation.

It must be fed, of course. It had for some hours taken but little, some soup from the buffet in the train—just-add-hot-water-and-serve canned soup, you know. A bottle of the most approved modification of the best of New York's milk product was given to the one-third of a year old infant. He engulfed it in the shortest possible time, while all the friends stood in a circle to see the beginning of the miraculous cure—a delivery from fading and wasting. He seemed to want more. His eye was brilliant, his look alert, he was truly something intellectual.

An incidental remark from the mother that he was "keeping this feeding down," enlightened me. He was accustomed, then, to spit up most of his food; she had scarcely finished when a sudden jet of milk, with high muzzle velocity, made the longest record-flight into air. He took four ounces and vomited, apparently, five. He was tired, excited; his stomach had revolted.

The baby was to be weaned from the mother's breast and fed on modified milk. The mother had practically no milk. The first prescription was a low average Walker-Gordon milk modification. After each feeding he habitually spat up little or much. His accustomed nurse took care of him. She was faithful, but not trained; not wise, but willing to obey.

It was gradually discovered that his feet were always cold, that he was most of the time wet, that he took his bottle rapidly, that he kept his food better at night. These were more points of information.

His feet warmed, his feedings given in a darkened room, his nurse soothing him and all his surroundings tranquil, he did somewhat better. He was thought to do better in the air. Central Park was near, and moderately quiet. All efforts to keep him from

ejecting some or all of his food failed and really for the moment the situation was discouraging. A week had passed and no real improvement. Indeed, the tiny thing was smaller and had lost his good humor. He wailed night and day, slept hardly at all. The pediatric household was depressed. No results toward cure, reputation going.

At this point a good child's nurse was found, one who not only was trained and experienced, but had some intuitive insight into the needs and comforts of an infant.

The instructions were to keep the baby in Central Park just as many hours a day as possible, eight hours not being considered too much. Fancy my surprise then on my return home about four o'clock to find the nurse and baby in the sunless backyard, north side of house, and that they had been there two or more hours. I was in an explosive mood, and making straight for the offending parties. Psh-psh-ee-ee-hh, was my greeting; a commanding look in the eye of the triumphant nurse made me pause. The child was getting its first sleep. For three and one-half hours that little moaning, starting, pale and wasted baby slept face downwards, lying across the arms and lap of the nurse. She had found Central Park too noisy. The sounds made the baby jump and wake. Here it was quiet. It would not sleep in its carriage, so she took it on her lap. At last she found it would sleep only in one position, viz., stomach down. For three and one-half hours the faithful little woman walked or casually sat a moment, gently soothing the worn-out nerves. For three and one-half hours it slept. It was its first good sleep. From that day the improvement began. From that moment the problem was solved. Nerve rest was imperative. The nurse saved the day, instructed the nurse maid, taught the doctor, cured the baby.

The exhibition of a four months' baby with nervous exhaustion, nervous dyspepsia, prostration, cured by a wise nurse, by rest treatment, is worth contemplation by all teachers and practitioners of pediatrics.

The recovery, of course, was slow. After three weeks it had gained three-quarters of a pound, was sleeping, taking good, large feedings of whole milk. From my house it sailed for Liverpool, was the only good sailor in the party, is now in rude health, is noisy and marring furniture.

After the diagnosis was made the early history of the infant was reviewed, and is as follows: The baby made a good start in life. After a few months social demands began to wear on the mother, and the milk suffered. In addition to all this was the incessant wear on the child's nerves. Their house was upon a most noisy trolley corner, where the din and clangor was so great that my backyard in New York City was like drowsy Cathay. The infant had many relatives, its full quota of grandparents, a great grandmother, many aunts and uncles. The young pair had hosts of friends, and all of them endowed with an inordinate superhuman fondness for babies. This found expression in waking the infant from sleep, kissing it, jumping it in the air, making it smile and coo and gurgle. It was an engaging baby and was most of the time engaged. The father had the pleasing habit of entering his own house with a bound, and discharging a war-whoop to announce himself to his young wife. This, of course, put an end to sleep and tranquility for the baby. Then followed a short gallop with the three to four months old infant, after which other affairs led the lord and master thence—unless perchance he met friends. If he did, he brought them in to see and jump and kiss the baby. By this time it was feeding time, if indeed the feeding had not been hastily engulfed in anticipation of the chance invasion.

It was noted as a precocious and pre-eminently cunning thing that this four months' son of the prize tandem driver should sit on his father's lap and lay his little white emaciated fingers on the lines as though driving. His rolling eyes looked out upon the kaleidoscopic mingling of human beings, horses and traps, "in such a sporty way," the mother said. Save the mark! A bulging-eyed marantic infant, starving and wasting, paraded by young, ignorant and proud parents, and calling him "sporty!"

This four-months-old baby was properly born, reasonably well started on the first months of life, nursed by its mother. By the third month it began to get thin, pale, to spit up food and by continuous, injudicious excitement and gradually failing breast food, soon got into a condition of nervous dyspepsia, until it finally was unable to retain and digest sufficient food to allow it to thrive, and was now wasting from starvation.

All this was corrected by quiet, the judicious care of a wise

nurse, a new-found, wise, soothing, comforting, quieting little woman, who liked the baby, took it naturally to her arms and enveloped it in such a warm embrace that it sank into a few short startled sleeps; then, finally, stretched out into one long relaxed infant's slumber, from which it emerged with sleepy winks and stretchings, the like of which it had scarce ever known. This first long sleep taught its lesson. Quiet surroundings were indicated. The infant was fed in a dark room. All bells, telephones and unnecessary noises were either muffled or reduced. Cotton was put in the infant's ears. Above all, this wise nurse was given sole charge of the infant. The presence of the father and friends were injurious to the child, the mother was too worn-out and nervous to be anything but harmful; the baby's usual nurse was also exhausted and nervous. The result was that in a fortnight the baby was feeding on maximum diet, sleeping perfectly and gaining weight.

It has thrived ever since. Last week a letter came announcing the fact that the baby was one year old and had eight teeth, and is "the finest colt in the paddock" (sporty father).

Another case is of much the same history. A young couple from the Southwest on their way to Newport stopped over in New York for a few days and wished to have the baby, five months old, examined in a routine way, to see that it was thriving and that all was being done for it that was possible. This sounds very noble and high-minded, but it really arose from a kind of vanity on the part of the parents. They thought that all, on seeing their infant, must throw up their hands in approval and applause.

Briefly, it was pale, thin, wide-eyed, alert, encircled under the eyes, starting, spitting up. Advice and admonition were accepted, but by no means appreciated. It was as though one were discussing ancient history; nothing said was taken to themselves.

On their return to New York, the child looked a little tanned, a little better, on the whole, but was nervous and spitting up food.

A friend confided to me that every day in Newport this father and mother went along the ocean drive in the crowded hours, in an automobile, with the baby facing forward and witnessing the parade. Not only that, but about half the time the proud father was tossing it, and facing it this way and that way, exclaiming: "See, see the wheels, see, baby, see the horses, see, SEE!" It was

even noted by the most dull that the mother and baby both looked nervous, starting and wide-eyed.

By the end of the season in Newport, the father was fairly well, the baby nearly worn out, and the mother quite finished. She left in a few weeks for the baths of Bohemia and spent a year recovering from seeing too many wheels and horses. I heard no more of the baby, but doubt not it is alive and a subject for Bohemian baths.

I think we all see certain members of a family, whose nervous systems are peculiarly sensitive to the nagging of other members. I spent a summer where a little girl was quite a painful exhibition of this. The girl was the youngest of three. The older were strong, stamping and tempestuous, fond of noise and confusion and accustomed to late hours. The youngest was thin, pale, quiet, sensitive, had an artistic temperament, was easily annoyed and teased, a poor sleeper. The older children goaded her without mercy. The parents, wholly oblivious of the situation, scolded her—worse than all, did not sympathize with her. She was like a little despairing, heart-broken thing, her nerves worn out, her sleep and digestion impaired, her only hope that the summer vacation would end and the family get busy enough with their usual home duties to leave her alone.

In February and March we see many cases of nervous exhaustion in school children. They are pale, jerky, choreic, talking in their sleep, sleeping too little, becoming dyspeptic.

This paper is to call attention to nervous exhaustion in infants. In the work of this Society it is desirable to teach the lesson of quiet surroundings, especially of allowing a certain quiet to initiate stomach digestion. It points to the necessity of close, constant watching, and individual-case-studying.

We need not interest ourselves with the mother who takes a year at the baths to recover from the strenuous life of the winter and summer. We should, however, try to protect the coming generation from nervous exhaustion, nervous dyspepsia, sleepless nights and choreic jerkiness before they have cut their first teeth.

DEPARTMENT OF ABSTRACTS

NEWTON, N. R. AND NEWTON, M.: RECENT TRENDS IN BREAST FEEDING. A REVIEW. (*American Journal of the Medical Sciences*, 221:691, June 1951).

The authors note the difference between the European and American attitudes toward the clinical importance of breast feeding. Studies indicate that breast-fed babies generally are subject to a lower risk of morbidity and mortality than those who are formula-fed. Introduction of formula feeding to infants in southern Egypt was a failure. In Switzerland, the morbidity rates for artificially-fed babies are reported to be twice those of the breast-fed. In the United States, formula-fed infants develop a significantly higher number of respiratory infections than do those who have been breast-fed for three or more months. For the feeding of premature infants most authorities are agreed that breast milk has special advantages. Whether erythroblastotic infants should be breast-fed by their mothers is a question that appears to be unsettled at the present time. Whether carcinogenic factors are present in human milk is an important and intriguing question. The transmission of mammary cancer in mice via a milk factor has been discussed. However, there is as yet no clear evidence that the same phenomenon occurs in the human.

MICHAEL A. BRESIA, M.D.

BROWN, T. MCP.; WICHELHAUSEN, R. H.; MERCHANT, W. R. AND ROBINSON, L. B.: A STUDY OF THE ANTIGEN-ANTIBODY MECHANISM IN RHEUMATIC DISEASES (*American Journal of the Medical Sciences*, 221: 618, June 1951).

Evidence has been presented which supports the basic theory of hypersensitivity in the pathogenesis of rheumatic diseases. There are indications that cortisone and ACTH block the antigen-antibody reaction without affecting the basic antigen. Studies utilizing human serum albumin have been initiated in the investigation of cortisone action. It has been suggested that the basic antigen in rheumatic diseases is a living agent, invisible in affected tissue and susceptible to the action of certain antibiotics. A parallel was found between the differential in vitro effect of these antibiotics on L organisms and their in vivo action on rheumatic subjects.

The observation reported lends support to the importance of a renewed interest in the microbiological approach in rheumatic and other collagen vascular diseases. We suggest that the antigen is capable of evoking a high degree of tissue hypersensitivity. This hypersensitivity may be increased by further induced antigen release with aureomycin, chloramphenicol and terramycin or suppressed by cortisone or human serum albumin. This new approach in the investigation of the basic mechanism in rheumatic disease must await prolonged clinical trial for final evaluation.

AUTHORS' SUMMARY.

SIMPSON, W. G.; ROSENBLUM, B. F.; WOOD, C. E. AND STAMMER, E. L.: LOCAL CORTISONE ACETATE THERAPY IN CONGENITAL SYPHILITIC INTERSTITIAL KERATITIS. (*Journal of Venereal Disease Information*: 32: 116, May 1951).

This is a preliminary report on nine cases of interstitial keratitis due to congenital syphilis in which cortisone acetate was used locally as an eye drop in conjunction with intramuscular penicillin. The patients ranged in age from 9 to 29. All but one had beneficial results. The cortisone acetate was prepared in a 1:4 dilution with normal saline and was used as an eye drop as follows: Two drops were instilled in each eye every hour during the waking hours for a period of 10 days. In addition to the cortisone each patient received 600,000 units of procaine penicillin intramuscularly daily for 12 days.

MICHAEL A. BRESCIA, M.D.

LAFF, H. I. AND ROBINSON, A.: IMPORTANCE OF BRONCHIAL INVOLVEMENT IN PRIMARY TUBERCULOSIS OF CHILDHOOD. (*Journal American Medical Association*, 146:778, June 30, 1951).

Bronchial involvement in the pathogenesis of parenchymal consolidation and in the course of primary tuberculosis in children is an important and frequently overlooked factor. Not only should bronchoscopic treatment be done in patients presenting evidence of wheezing, atelectasis or obstructive emphysema but in every patient with childhood primary pulmonary tuberculosis whose progress is not considered satisfactory. The relative ease and safety of bronchoscopic examination in such patients is stressed, as well as some of the complications found in later life that might be averted.

AUTHORS' SUMMARY.

HARTMAN, E. E. AND KENNEDY, R. L. J.: ILLNESS IN THE FIRST TRIMESTER OF PREGNANCY. ITS LACK OF SIGNIFICANCE IN RELATION TO CONGENITAL ANOMALY OF THE OFFSPRING AND TO FULL-TERM PREGNANCY, PREMATURITY AND STILLBIRTH. (*Journal of Pediatrics*, 38:306, March 1951).

Of 1,228 mothers who gave birth to 1,237 infants in 1948, 148 mothers were ill at some time in the first trimester of pregnancy. These ill mothers subsequently gave birth to 149 children, 8 of whom (5.4 per cent) had congenital anomalies. The 1,080 mothers who were not ill in the first trimester of pregnancy gave birth to 1,088 infants of whom 57 (5.2 per cent) had congenital anomalies. Thus, there was no significant difference between the incidence of congenital anomalies following maternal illness in the first trimester of pregnancy and that following uneventful pregnancy. Furthermore, whether or not the mothers were ill in the first trimester of pregnancy apparently made no significant difference in the incidence of full-term pregnancy, prematurity or stillbirth.

AUTHORS' SUMMARY.

ASTRUP, P.; BROCHNER-MORTENSEN, K.; FABER, V.; HAMBURGER, C.; HARBOE, N.; SCHMITH, K.; SNORRASON, E.; SPRECHLER, M., AND VESTERDAL, J.: THE EFFECTS OF ADRENOCORTICOTROPHIC HORMONE (ACTH) IN A CASE OF JUVENILE RHEUMATOID ARTHRITIS. (*Acta Paediatrica*, 39:215, 1950).

A 10-year-old girl with rheumatoid arthritis was treated with ACTH. At first a marked clinical improvement was noted, together with a decrease in the sedimentation rate to normal. The treatment was continued with very small doses (2 mg. daily) for a month. The sedimentation rate soon rose to the original value, but a clinical relapse was not seen until the end of this first period. Another course was started with larger doses of a new batch of ACTH without any effect on the clinical condition or the erythrocyte sedimentation rate. After a few days' treatment, albuminuria developed, followed by a severe nephrosis. During treatment the serum protein, the serum uric acid and nonspecific hyaluronidase inhibitor in serum decreased. Hyperglycemia and glycosuria occurred to a light extent. There were no significant alterations of serum K, Na, Ca, Cl, blood cholesterol, phosphatase, urea, plasmin, plasminogen or antiplasmin. The hemoglobin, W.B.C. and a num-

ber of circulating lymphocytes increased, while the eosinophiles decreased. During the first period of high dosage the excretion of both 17-keosteroids and glucocorticoids increased, but during the last period, when almost no clinical effect was seen, only the former increased.

MICHAEL A. BRESCIA, M.D.

CONYBEARE, E. T., AND LOGAN, W. P. D.: THE INCIDENCE AND PREVENTION OF TETANUS AMONG CIVILIANS. (*British Medical Journal*, 4705:504, March 10, 1951).

A review of the mortality statistics of tetanus among civilians in England and Wales (1927-1948) shows that during this period mortality was highest during infancy and childhood, lowest during the middle years of life, and rose again after 50 years, especially among the males. Tetanus male death rates at all ages are much higher than the corresponding females rates. Fatal infantile tetanus is almost entirely a disease of the neonatal period. Death rates are higher in the rural districts. The authors suggest that active immunization of children at about the age of entry to school would be both practicable and justified.

MICHAEL A. BRESCIA, M.D.

PLUM, F., AND LUKAS, D. S.: AN EVALUATION OF THE CUIRASS RESPIRATOR IN ACUTE POLIOMYELITIS WITH RESPIRATORY INSUFFICIENCY. (*American Journal of the Medical Sciences*, 221:417, April 1951).

The effects of a cuirass respirator have been evaluated on 10 patients with respiratory insufficiency due to acute poliomyelitis. Two patients were studied during their acute illness, 5 patients were studied during convalescence while they still needed artificial respiration, and 3 patients were examined at autopsy. Blood acidosis, due to failure of carbon dioxide elimination from the lungs, was a manifestation of respiratory insufficiency in 2 acutely ill patients, and occurred in the absence of anoxemia. Respiratory acidosis was not prevented or corrected in these 2 acutely ill patients with artificial respiration with a cuirass respirator, but was at least partially corrected by tank respirators. Tank respirators produced from 34 to 100 per cent greater tidal volumes at equivalent pressures than did a cuirass respirator on 5 convalescent

patients with paralyzed respiratory musculatures. Anterior pulmonary emphysema was seen at postmortem examination in the 3 patients who died following treatment in the cuirass respirator. Only when the advantages offered by the cuirass respirator was compelling, and when the amount of ventilation produced can be determined to be physiologically sufficient, does it seem desirable to use this device in its present stage of development.

AUTHORS' SUMMARY.

TREATMENT OF LEUKEMIA AND OF HODGKIN'S DISEASE. (Folia Haematologica, Leipzig, 70: 59, 1950). Because sulfonamides inhibit the growth of bacteria, an investigation was made to determine whether they also had an inhibiting effect on cells of the human body. It was shown in healthy subjects and in patients with infectious diseases that the administration of sulfonamides nearly always produces a decrease in the leukocyte count, which suggests that sulfonamides curtail granulopoiesis and shorten the life span of granulocytes in the peripheral blood. This is in accord with the observation that sulfonamides occasionally produce agranulocytosis. The effect of paraaminobenzoic acid on the leukocytes was also investigated. It was found to cause an increase in the leukocyte count. It became apparent that the leukocyte test is a valuable biologic test that provides an insight into the mode of action of certain inhibiting and growth substances. The cytostatic effect of sulfonamides induced the author to try sulfonamides in the treatment of leukemia and Hodgkin's disease (lymphogranulomatosis). On the basis of observations in 83 cases of leukemia, he says that if sulfonamide medication is used in combination with roentgen irradiation, the progressive course of leukemia can be retarded. In lymphatic leukemia the therapeutic effects are more promising than in myeloid leukemia. In Hodgkin's disease ultimate cure seems possible if the sulfonamides and roentgen therapy are employed in combination and for a long period of time. The average life expectancy has been significantly increased in Hodgkin's disease. Sulfathiazole has proved the most effective among the sulfonamides. The author also briefly mentions the use of choline in the treatment of tumors.—*Journal A.M.A.*

ITEMS

TRIAL OF CINCHONIMIC ACID DERIVATIVE. (British Medical Journal, 1: 383, Feb. 24, 1951). Twelve patients, nine adults and three children, four with rheumatic fever, two with polyarteritis nodosa, three with scleroderma and three with lupus erythematosus were treated with a cinchonimic acid derivative, 3-hydroxy-2-phenylcinchonimic acid. The dosage used was 20 mg. per kilogram of body weight by mouth daily, which in some instances was increased to 40 mg. Seven patients were treated for one week, the remaining five patients for two or three weeks. The drug was taken after breakfast in three divided doses at hourly intervals. Fever and acute arthritis were speedily relieved in the patients with rheumatic fever. Results in polyarteritis nodosa were equivocal. The most striking effects were obtained in the patients with scleroderma, a disease hitherto not responsive to any known treatment. Improvement occurred in all three patients, as shown microscopically by biopsy specimens obtained before and after treatment. The results have so far been maintained in one patient and were only temporary in the other two. Slight and inconstant improvement followed the administration of the 3-hydroxy-2-phenylcinchonimic acid in chronic lupus erythematosus but was not confirmed by microscopic examination. Toxic effects were infrequent and less severe than those that may follow the use of sodium salicylate and consisted in slight nausea, diarrhea, and, more rarely, vomiting.—*Journal A.M.A.*

TREATMENT OF RHEUMATIC FEVER. (Revista Argentina de Reumatología, Buenos Aires, 15: 232, Feb. 1951). Schnir administered rutin and ascorbic acid to 15 patients of either sex between the ages of 10 and 60 with rheumatic fever. Four patients were seen during the first month in the first attack of the disease. They had normal hearts. Eleven patients were seen during a recurrence of rheumatic fever. The number of recurrences in these patients varied between one and six. Ten of the patients had a cardiac lesion that was clinically and/or roentgenologically demonstrated. Rutin was given every four hours in five fractional doses varying

from 60 to 250 mg. each. Ascorbic acid was given in two fractional doses of 250 or 500 mg. morning and night. The total dose of rutin varied between 5 and 60 gm. The total dose of ascorbic acid varied between 8 and 60 gm. Cure was obtained in all patients, as manifested by control of fever and of cutaneous, visceral, and articular symptoms, reduction of the erythrocyte sedimentation rate, and stabilization or disappearance of clinical, roentgenologic, and electrocardiographic evidence of cardiac disease. Within the first three months after discontinuation of treatment the patients had a recurrence that was controlled by repeated treatment up to a total dose of 500 mg. of rutin and 500 mg. of ascorbic acid. Rutin and ascorbic acid are not followed by toxic reactions or unpleasant late results. The substances potentiate the effect of each other, diminish the permeability of the tissues, and act favorably on the heart disease.—*Journal A.M.A.*

INFECTIOUS MONONUCLEOSIS. (Deutsche medizinische Wochenschrift, Stuttgart, 76: 205, Feb. 16, 1951). Infectious mononucleosis appeared in epidemic proportions at a hospital in Kiel during the spring of 1950. However, in many cases a correct diagnosis was established only on the basis of the differential blood picture. This was the case in 15 of 63 patients who had been hospitalized with a diagnosis of diphtheria or suspected diphtheria. Since only patients who were suspected of diphtheria were hospitalized, it is likely that numerous other patients with infectious mononucleosis were treated elsewhere under different diagnoses, especially since the symptomatology of the disease varies widely. Three different forms are usually differentiated: (1) Pfeiffer's glandular fever, with generalized swelling of lymph nodes (usually occurring in young children); (2) the anginal form (monocytic angina), and (3) the purely febrile form, in which general symptoms predominate. In 13 of the 15 patients reported on here, anginal symptoms predominated, the other two (both children of 18 months) had the symptoms characteristic of Pfeiffer's glandular fever. The importance of the heterophilic antibody reaction of Paul-Bunnel is explained. A positive reaction corroborated the diagnosis in 11 of the 15 cases here reported. In seven instances punctates of lymph nodes or tonsils were examined for further clarification of the diag-

nosis. This measure which has been recommended by Lämmler, yielded satisfactory results in only three of the cases, and so the author feels that this diagnostic aid can be dispensed with.

—*Journal A.M.A.*

CHLORAMPHENICOL IN TREATMENT OF TYPHOID OR PARATYPHOID. (Semaine des Hôpitaux de Paris, 27: 630, Feb. 26, 1951). Forty nursing infants and children with typhoid or paratyphoid were treated with chloramphenicol (chloromycetin[®]). Nursing infants and small children were given orally 0.05 to 0.10 gm. of the drug per kilogram of body weight. Older children received a total dose of 1.5 to 2 gm. daily. Treatment with these doses administered in tablets was continued for eight to 15 days. Untoward reactions reported by others, such as collapse or severe digestive disturbances resulting in death, were not observed by the authors. They caution against a massive initial dose of the drug and advise administration of half the dose for the first two days of treatment. With this technique, fever may be prolonged (from two to five days), but typhoid deaths, which were already few in children before antibiotic therapy was instituted, may be eliminated. In the authors' patients rapid defervescence occurred within seven days and frequently within four days. Recovery without sequelae resulted in two patients with severe typhoid encephalitis. Nearly complete recovery from typhoid osteomyelitis of the metacarpus and phalanges occurred in one instance. Only two of the 40 patients had recurrences. Serum diagnosis was made on a strongly positive Widal reaction in all instances, which appeared after the usual interval.—*Journal A.M.A.*

Medal of Honor



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Singer, E. I., Michael, J., Monk, F. C., and Kirby, W. M. B., *J. Am. Med. Ass.* 221:1254 (March) 1969.

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